SYNTHESIS AND STUDY OF PROPERTIES OF AZOLES

AND THEIR DERIVATIVES

COMMUNICATION 22. SYNTHESES BASED ON 1-ADAMANTANECARBONITRILE

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Only a limited amount of information exists in the literature on imidazolines, benzimidazoles and other azoles that contain adamantyl radicals. In the present paper we describe the preparation of a number of heterocyclic compounds based on 1-adamantanecarbonitrile (I).

Despite the fact that nitriles of the adamantane series are known, the simplest nitrile (I) was not described prior to our work. Compound (I) was obtained from 1-adamantanecarboxamide, which was synthesized as described in [1-3]. When refluxed with $SOCl_2$ in benzene the amide is converted almost quantitatively to (I). The hydrochlorides of the imino esters of 1-adamantanecarboxylic acid, (II) and (III), were obtained by the Pinner reaction, by the reaction of (I) with either methanol or ethanol in the presence of dry HCl

$$AdC \equiv N + ROH + HCl \rightarrow AdC$$
(I)
$$R = CH_{3} (11), C_{2}H_{5} (111)$$

Ad is the adamantyl radical here and subsequently.

It should be mentioned that the formation of (II) and (III) proceeds with much more difficulty than when ordinary aliphatic nitriles are used, from which the hydrochlorides of the imino esters are usually formed immediately after the mixture of nitrile and alcohol is saturated with HCl, or else within several hours. In the case of (II) and (III) this requires 4-5 days.

As is known, the stability of the hydrochlorides of the imino esters depends on the character of the substituent attached to the $C(=NH \cdot HCl)OR$ grouping. If this substituent has an electron-acceptor character, then the hydrochlorides of the imino esters are unstable [4, 5]. Substituents that are electron donors increase the stability of the imino ester hydrochlorides. The adamantyl radical is a strong electron donor and, as a consequence of this, hydrochlorides (II) and (III) are stable crystalline compounds that, in the absence of moisture, can be stored for a long time under ordinary conditions without manifesting any signs of decomposition.

The structure of (II) and (III) was confirmed by the elemental analysis data, and also by the reactions that are characteristic for the hydrochlorides of imino esters: the Pinner rearrangement, hydrolysis, and conversion to the free imino ester.

The Pinner rearrangement — the conversion of $RC(=NH \cdot HCl)OR'$ to $RCONH_2$ and R'Cl when heated — is an S_N2 process that is strongly dependent on steric hindrance. The adamantyl radical creates much steric hindrance for the Pinner rearrangement. In addition, this process is hindered by the electron-donor character of the adamantyl radical. For this reason (II) decomposes with fairly high speed only at temperatures >170°C.

I. M. Gubkin Institute of the Petrochemical and Gas Industry, Moscow. N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 144-148, January, 1974. Original article submitted June 20, 1973.

• 1974 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00. The hydrolysis of (II) and (III) proceeds at room temperature and leads to the 1-adamantanecarboxylic acid esters (V) and (VI). The treatment of a suspension of (II) in ether with an equivalent amount of Et_3N at 0-5° gives the methyl imino ester of 1-adamantanecarboxylic acid (VII).



When the IR spectrum of (VII) is examined the attention is attracted to the noticeable shift of the band that is characteristic for the stretching vibrations of the C = N bond. If for the methyl imino esters of carboxylic acids the absorption bands for the C = N bond lie in the 1655-1660 cm⁻¹ region, then in the IR spectrum of (VII) this band is shifted to 1640 cm⁻¹. In order to identify it, (VII) was converted to the starting (II) by treatment with dry HCl in ether.

The condensation of (II) with ethylenediamine was accomplished in absolute methanol, as a result of which 2-(1'-adamantyl)imidazoline (VIII) was obtained in 92% yield. In a similar manner, 2-(1'-adamantyl)-benzimidazole (IX) was obtained in 71% yield from a mixture of equivalent amounts of (II) and o-phenylene-diamine. The reaction of (II) with o-aminophenol gave 2-(1'-adamantyl)benzoxazole (X) in 76% yield. The long heating of (VII) with ethanolamine at 180°, until the NH₃ evolution ceased, gave 2-(1'-adamantyl)oxazoline (XI) in 93% yield.

It seemed interesting to effect the trimerization of (VII) to the triazine. A product that was identical with (I) was isolated after the free imino ester (VII) was heated with 5% of (II) at 180° for 8 h. Absorption bands in the 1555 cm⁻¹ region, characteristic for the triazine ring, were absent in the IR spectrum of the obtained product, and instead an absorption band was observed at 2225 cm⁻¹, which corresponds to the vibrations of the $-C \equiv N$ group.

The inability of (VII) to undergo cyclotrimerization to the triazine can be explained, on the one hand, by the effect of the electron-donor adamantyl radical, and on the other hand, by the steric hindrance created by the adamantyl radical.

EXPERIMENTAL METHOD

The IR spectra were taken on a UR-10 instrument.

1-Bromoadamantane was obtained as described in [1], mp 113-115°. 1-Adamantanecarboxylic acid was obtained as described in [2], mp 181°. The acid chloride of 1-adamantanecarboxylic acid was obtained as described in [2]. It was not purified for the further transformations. 1-Adamantanecarboxamide was obtained as described in [3], mp 188-189°.

 $\frac{1-A damantane carbonitrile (I)}{ml of absolute benzene was refluxed for 10 h, cooled to ~20°, poured over 25 g of ice, and then 50% aqueous NaOH solution was added until weakly alkaline. The mixture was extracted with ether, the ether$

solution was washed with water, dried over Na_2SO_4 , and the solvent was removed in vacuo. We obtained 1.56 g (97%) of (I), mp 191-192° (from aqueous methanol). Found: C 82.42; H 9.54; N 9.09%. $C_{11}H_{15}N$. Calculated: C 81.98; H 9.28; N 8.74%. Infrared spectrum (ν , cm⁻¹): 2225 (C = N).

Hydrochloride of Methyl Imino Ester of 1-Adamantanecarboxylic Acid (II). A stream of dry HCl was passed through a solution of 1.61 g of (I) and 0.32 g of absolute methanol in 40 ml of absolute ether at 0-5° for 1.5-2 h, after which the mixture was allowed to stand for a day at ~20°, and then for three days at 0°. The obtained crystalline precipitate was filtered, washed with absolute ether, and dried in a vacuum-desiccator over NaOH. We obtained 1.7 g (75.3%) of (II), mp 182-183° (from a CH_3COOH -ether mixture). Found: Cl 15.55%. $C_{12}H_{20}NOCl$. Calculated: Cl 15.47%.

Hydrochloride of Ethyl Imino Ester of 1-Adamantanecarboxylic Acid (III). A stream of dry HCl was passed through a solution of 0.8 g of (I) and 0.22 g of absolute ethanol in 10 ml of absolute ether at 0-5° for 1 h. The mixture was allowed to stand for a day at ~20°, and for three days at 0°. The ether and excess HCl were removed in vacuo. The obtained crystalline precipitate was filtered, washed with absolute ether, and dried in a vacuum-desiccator over NaOH. We obtained 0.8 g (66%) of (III), mp 174-175°. Found: Cl 15.24%. C₁₃H₂₂NOCl. Calculated: Cl 14.98%.

Thermal Decomposition of Hydrochloride of Methyl Imino Ester of 1-Adamantanecarboxylic Acid. One gram of (II) was heated at $180-190^{\circ}$ until the CH₃Cl evolution ceased, after which it was kept at this temperature for an additional 15 min. The reaction mass was extracted with absolute benzene, and the solvent was removed in vacuo. We obtained 0.7 g (89%) of 1-adamantanecarboxamide (IV), mp 188-189° (from cyclohexane); cf. [3].

Saponification of Hydrochloride of Methyl Imino Ester of 1-Adamantanecarboxylic Acid. To a suspension of 0.23 g of (II) in 20 ml of ether was added 30 ml of water, and the mixture was stirred vigorously for 8 h at ~20°. The ether layer was separated, and the aqueous layer was extracted with ether. The ether layer and ether extracts were combined, dried over MgSO₄, and the solvent was vacuum-distilled. We obtained 0.16 g (85%) of the methyl ester of 1-adamantanecarboxylic acid (V), mp 36° (from hexane); cf. [6].

Saponification of Hydrochloride of Ethyl Imino Ester of 1-Adamantanecarboxylic Acid. To a suspension of 0.17 g of (III) in 20 ml of ether was added 6 ml of water, after which the mixture was stirred vigorously for 29 h at ~20°, worked up as described for (V), and the product was distilled. We obtained 0.1 g (66%) of the ethyl ester of 1-adamantanecarboxylic acid (VI), bp 112° (5 mm); cf. [1].

Methyl Imino Ester of 1-Adamantanecarboxylic Acid (VII). With stirring, to a suspension of 6.87 g of (II) in 60 ml of absolute ether was gradually added at $0-5^{\circ}$ a solution of 3.04 g of Et₃N in 20 ml of absolute ether. The reaction mixture was stirred for 2 h at 5°, and the precipitate was filtered and washed with absolute ether. After removal of the solvent the residue was fractionally distilled. We obtained 4.22 g (71.3%) of (VII), bp 115-116° (5 mm); nD²⁰ 1.5108; d4²⁰ 1.3968. Found: C 74.49; H 9.74; N 7.52%. C₁₂H₁₉ON. Calculated: C 74.57; H 9.82; N 7.24%. Infrared spectrum (ν , cm⁻¹); 1640 (C = N), 3350 (NH).

2-(1'-Adamantyl)imidazoline (VIII). With stirring, 2.29 g of (II) was added at 0° to a solution of 0.6 g of ethylenediamine in 25 ml of absolute methanol. After stirring at this temperature for 1 h the reaction mixture was refluxed for 2 h, cooled to 0°, and a solution of 0.23 g of Na in 10 ml of absolute methanol was added gradually at 0°. The obtained precipitate was filtered, and the filtrate was evaporated to dryness. We obtained 1.88 g (92%) of (VIII), mp 165-166° (from alcohol). Found: C 76.47; H 9.78; N 13.87%. $C_{13}H_{20}N_2$. Calculated: C 76.42; H 9.86; N 13.72%. Picrate, mp 172-173° (from aqueous methanol). Infrared spectrum (ν , cm⁻¹): 1290 (C—N), 1630 (C = N), 1450 (CH₂, "scissors" vibrations in imidazoline ring).

2-(1'-Adamantyl)benzimidazole (IX). A mixture of 1.15 g of (II) and 0.54 g of o-phenylenediamine in 30 ml of absolute methanol was refluxed for 1 h, cooled, and poured with stirring into cold water that contained an equivalent amount of NaHCO₃. The obtained precipitate was filtered, washed with water, and dried in a vacuum-desiccator over NaOH. We obtained 0.9 g (71.5%) of (IX), mp >300° (from aqueous methanol). Picrate, mp 253-254° (from methanol); cf. [7]. Infrared spectrum (ν , cm⁻¹): 1650 (C = N), 1280 (C-N), 1410 (C = C), 750 (out-of-plane deformation vibrations of C-H in 1,2-disubstituted benzene derivatives).

2-(1'-Adamantyl) benzoxazole (X). A mixture of 1.15 g of (II) and 0.55 g of o-aminophenol in 30 ml of absolute methanol was refluxed for 1 h, cooled, and poured into cold water that contained an equivalent

amount of Na₂CO₃. The obtained precipitate was filtered, washed with water, and dried in a vacuum-desiccator. We obtained 0.96 g (76%) of (X), mp 133° (from aqueous alcohol). Found_ C 80.92; H 7.61; N 5.38%. $C_{17}H_{19}NO$. Calculated: C 80.39; H 7.85; N 5.52%. Infrared spectrum (ν , cm⁻¹): 1250 (C-O-C), 750 (out-of-plane deformation vibrations of C-H in 1,2-disubstituted benzene derivatives).

<u>2-(1'-Adamantyl)oxazoline (XI)</u>. A mixture of 0.5 g of (VII) and 0.15 g of ethanolamine was heated at 180° for 16 h until the NH₃ evolution ceased. The obtained product was dissolved in methanol, refluxed with active carbon for 1.5 h, filtered, and the filtrate was evaporated in vacuo. The residue was purified twice by passage through a column filled with Al_2O_3 (II activity). We obtained 0.48 g (93%) of (XI) as a light brown waxy mass. Picrate, mp 217-218° (from alcohol); cf. [7]. Infrared spectrum (ν , cm⁻¹): 1645 (C = N), 1275 (C-O-C).

CONCLUSIONS

1. 1-Adamantanecarbonitrile reacts with alcohols and hydrogen chloride with greater difficulty than do aliphatic nitriles to give the hydrochlorides of the imino esters of 1-adamantanecarboxylic acid, which are more stable than the corresponding compounds of the aliphatic series.

2. The hydrochloride of the methyl imino ester of 1-adamantanecarboxylic acid condenses with ethylenediamine, o-phenylenediamine and o-aminophenol in the usual manner to give the corresponding heterocyclic compounds.

3. The methyl imino ester of 1-adamantanecarboxylic acid when heated with ethanolamine gives the corresponding oxazoline. The hydrochloride of the methyl imino ester of 1-adamantanecarboxylic acid does not give the s-triazine when heated, and instead gives 1-adamantanecarbonitrile.

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